

No analgesic can yet be thought to be completely free of possible nephrotoxicity, and patients on long-term treatment with combined analgesics may be particularly susceptible to RPN.

We thank Dr S Callender for permission to report this case, and Dr J G G Ledingham for his help.

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<sup>2</sup> Stewart, J H, and Gallery, E, *Australian and New Zealand Journal of Medicine*, 1976, **6**, 498.  
<sup>3</sup> Murray, T, and Goldbury, M, *Annual Reviews of Medicine*, 1975, **26**, 537.  
<sup>4</sup> Nanra, R S, and Kincaid-Smith, P, *British Medical Journal*, 1970, **3**, 559.  
<sup>5</sup> New Zealand Rheumatism Association Study, *British Medical Journal*, 1974, **1**, 593.

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## Convulsions and hyperglycaemia associated with nalidixic acid

Hyperglycaemia and convulsions in patients taking nalidixic acid are usually associated with overdosage of the drug or an underlying epileptic tendency.<sup>1-3</sup> Nalidixic acid may also interfere with biochemical determinations of plasma and urinary glucose, giving false-positive results. We describe an otherwise healthy patient who had convulsions and hyperglycaemia (confirmed by a glucose-specific method<sup>4</sup>) while on a therapeutic dose of the drug.

### Case report

A 31-year-old housewife wakened 30 minutes after falling asleep, feeling giddy and complaining of a headache and a buzzing noise in her head. Soon afterwards she developed generalised jerking of her limbs, which was subsequently clearly described by her husband, although she had no recollection of these events. Over the next 45 minutes she had recurrent convulsions, and between attacks was unresponsive, although mumbling incoherently and sweating profusely. She was not incontinent and did not bite her tongue.

Two days before she had been started on a course of nalidixic acid (Negram), 1 g four times daily, for urinary frequency and dysuria. Apart from oral contraceptives (Ovulen 50), which she had been taking for over a year, she was not taking any drugs. There was no history of alcohol intake, no evidence of drug overdose, and no family history of diabetes mellitus or epilepsy.

She looked unwell, pale, and tired, but no abnormality was found in any system, and neurological examination in particular gave normal results. Urine analysis (Labstix) showed ketonuria ++, proteinuria +, and glycosuria ++++. Clinitest detected the presence of 1% reducing substances. Blood glucose on admission was 10.8 mmol/l (195 mg/100 ml), urea 5 mmol/l (30 mg/100 ml), sodium 136 mmol(mEq)/l, potassium 3.7 mmol(mEq)/l, and total CO<sub>2</sub> 24 mmol/l (11 ml/100 ml). The white cell count was raised at 14.3 × 10<sup>9</sup>/l (14 300/mm<sup>3</sup>), including 81% neutrophils, but other haematological values were normal. Urine cultures were sterile, and an intravenous pyelogram and creatinine clearance test showed nothing abnormal. A standard 50-g oral glucose tolerance test carried out four days later also gave a normal result.

Drug treatment was discontinued after admission, and she made an uneventful recovery. An electroencephalogram on the day of admission showed minor non-specific bilateral episodic abnormalities, but further recordings taken five days and three months later were both within normal limits. A computerised brain scan (EMI) also showed no abnormality. After discharge she had no further convulsions.

### Comment

Between 1964 and 1975 eight episodes of convulsions associated with nalidixic acid were reported to the Committee on Safety of Medicines,<sup>1</sup> and to 1971 three examples had been reported in Australia.<sup>2</sup> Standard pharmacological textbooks, however, record this side effect only in patients with conditions such as Parkinsonism, cerebrovascular insufficiency, or pre-existing epilepsy. Other reports associate convulsions with high or excessive doses only.

Islam and Sreedharan<sup>3</sup> reported convulsions, hyperglycaemia, and glycosuria due to nalidixic acid, but their patient was a 14-year-old girl who had taken an overdose of 6.5 g of the drug. Klumpp<sup>5</sup> observed that the hyperglycaemia and glycosuria could both be false-positive results, since glucuronides of nalidixic acid present in urine can produce free glucuronic acid which acts as a reducing agent. In our patient, however, the method used to detect glycosuria (Labstix), and the assay that confirmed hyperglycaemia were specific for glucose.<sup>4</sup>

We found no evidence of any epileptic tendency or underlying cerebral dysfunction in our patient, and conclude that even normal doses of nalidixic acid may cause convulsions in perfectly healthy people, probably as an idiosyncratic adverse reaction.

We thank Dr D A Seaton for permission to report this case.

<sup>1</sup> Committee on Safety of Medicines. Personal communication.

<sup>2</sup> *Medical Journal of Australia*, 1972, **1**, 435.

<sup>3</sup> Islam, M A, and Sreedharan, T, *Journal of the American Medical Association*, 1965, **192**, 1100.

<sup>4</sup> Telfer Brunton, W A, and Percy-Robb, I W, *Clinica Chimica Acta*, 1976, **69**, 131.

<sup>5</sup> Klumpp, T G, *Journal of the American Medical Association*, 1965, **193**, 746.

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## SHORT REPORTS

### Alpha and beta coma in drug intoxication

The electroencephalogram (EEG) has long been used in evaluating the comatose patient. The finding of alpha activity in the EEG in some patients in coma has aroused increasing interest, this being a pattern normally associated with wakefulness.<sup>1-2</sup> This seemingly paradoxical combination of behavioural and electroencephalographic features has been termed "alpha coma" and has been seen mainly in cases of pontomesencephalic infarction or diffuse posthypoxic cerebral cortical necrosis. With few exceptions the prognosis in such cases has been dismal.<sup>3</sup> Little has been published on alpha coma occurring in drug intoxication. We have recently seen four patients who were rendered comatose or stuporous by overdoses of nitrazepam or chlormethiazole

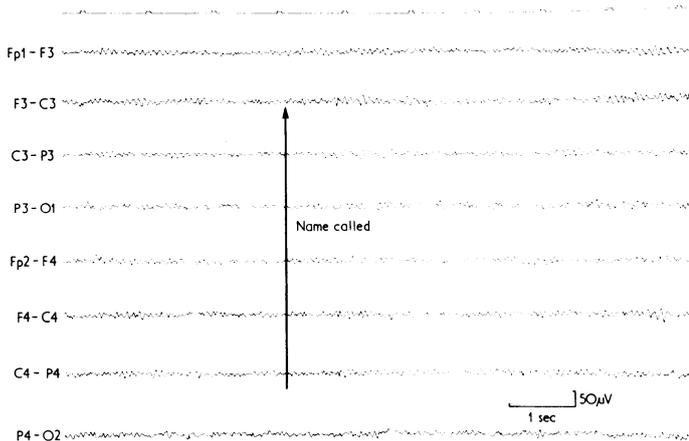
in whom the EEG was dominated by frequencies in the alpha or slow beta range. Each made a complete recovery without neurological sequelae.

### Patients and results

A 41-year-old man was rendered comatose by an overdose of nitrazepam. Corneal, gag, and ocular motor reflexes were absent on admission, but pupillary responses were preserved. There was generalised hyporeflexia and hypotonia, and plantar responses could not be elicited. The EEG on admission comprised generalised 10 Hz alpha activity, which was most prominent in the frontal and central regions. This activity did not attenuate with the application of painful, auditory, or visual stimuli. Gradually deepening respiratory depression without appreciable hypoxaemia prompted ventilatory assistance, which was continued for the next 36 hours without further sedation. During this period, together with recovery of brainstem

reflexes, the alpha activity in the EEG slowed to 8 Hz and maintained the frontal distribution but attenuated for short periods in response to stimulation. Forty-eight hours after admission the patient was alert. The final EEG performed three weeks later as an outpatient showed normally reactive 10 Hz alpha activity in a posterior distribution.

The other three patients were all receiving chlormethiazole for alcohol withdrawal states. Two had generalised seizures, and all three were treated with thiamine and diazepam, and one with phenytoin and phenobarbitone. Each of the three had biochemical evidence of hepatic dysfunction, and one had mild transient hyperammonaemia. Two became comatose and one stuporous shortly after starting high doses of chlormethiazole. The initial EEGs of all three patients showed generalised or predominantly frontal alpha or slow beta activity, which did not react to the usual alerting stimuli. In the two comatose patients the activity was in the 11-12 Hz frequency range in one (see figure) and in the 12-14 Hz range in the other. The third patient, who also received phenytoin and phenobarbitone, showed frontally predominant 14-16 Hz beta activity. Withdrawal of the chlormethiazole was accompanied by a return to normal consciousness with normally reactive posterior alpha activity and beta frequencies in the EEG in each case.



Generalised non-reactive 11-12 Hz alpha activity in EEG of comatose 54-year-old man after chlormethiazole administration for alcohol withdrawal.

**Comment**

Alpha coma has usually carried a poor prognosis despite a recent report by Grindal *et al*<sup>3</sup> of nine survivors from a series of 24 cases. Although generalised beta activity is well recognised in certain forms of drug-induced coma,<sup>4</sup> and has also been reported in non-comatose patients receiving chlormethiazole for alcohol withdrawal,<sup>5</sup> to our knowledge alpha coma has not been described in association with benzodiazepine or chlormethiazole intoxication.

The present cases raise several points of practical importance. Firstly, the finding of diffuse or frontally predominant non-reactive alpha activity in the EEG of a patient in coma does not necessarily indicate structural brain disease but should also suggest a possible pharmacological cause. Secondly, the observation of this type of EEG pattern in patients with profound drug-induced coma need not imply that secondary hypoxic brain damage has occurred. Finally, the present cases illustrate the variability of the EEG changes produced by chlormethiazole when used with other drugs during alcohol withdrawal.

We conclude that when the EEG shows the dominant activity to be in the alpha and beta range of frequencies in patients in coma due to drug intoxication, uncomplicated by appreciable cerebral hypoxia, a favourable outcome is to be expected.

<sup>1</sup> Loeb, C, Rossadini, G, and Poggio, G F, *Neurology*, 1959, **9**, 610.  
<sup>2</sup> Westmoreland, B F, *et al*, *Archives of Neurology*, 1975, **32**, 713.  
<sup>3</sup> Grindal, A B, Suter, C, and Martinez, A J, *Annals of Neurology*, 1977, **1**, 371.  
<sup>4</sup> Konigshausen, Th, and Rabe, F, *Medical World*, 1975, **26**, 1655.  
<sup>5</sup> Bergener, M, *Acta Psychiatrica Scandinavica*, 1966, **42**, suppl 192, 65.

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# Atrial fibrillation complicating Wolff-Parkinson-White syndrome treated with amiodarone

A patient with Wolff-Parkinson-White (WPW) syndrome may be at risk if atrial fibrillation occurs. The myocardial bridge that bypasses the atrioventricular node transmits impulses at a very rapid rate if its refractory period is short: the ventricular response may then be fast enough to endanger life. Paradoxically, digitalis may shorten the refractory period and be hazardous by increasing ventricular rate during atrial fibrillation.<sup>1</sup> Other conventional drugs such as beta-adrenoceptor blocking agents may also be ineffective or contraindicated, and many cases have been refractory to medical treatment. We report the first use of amiodarone in Britain, and the patient has been successfully controlled for nearly four years.

**Case report**

In June 1973 a 75-year-old man presented after 10 weeks of palpitation and breathlessness that had not responded to digoxin, 0.75 mg daily, and frusemide. The patient looked younger than his years but was cyanosed and severely dyspnoeic with severe congestive heart failure. His heart rate was irregular at 180/min. There was radiological evidence of cardiomegaly and pulmonary oedema. The electrocardiogram showed rapid atrial fibrillation with anomalous AV conduction (WPW syndrome type B). The plasma digoxin concentration suggested serious toxicity at 6 ng/ml.

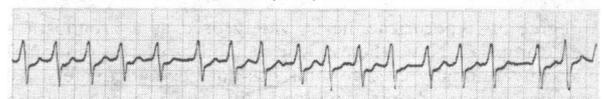
Increased diuretic treatment, verapamil, and practolol, and reduction in digoxin dosage all proved ineffective. Quinidine slowed the ventricular rate and restored sinus rhythm, but after seven days a widespread erythematous rash developed; the rhythm reverted to atrial fibrillation within 24 hours of withdrawing the drug. Procainamide, phenytoin, and mexiletine were tried separately and in various combinations. The patient was discharged on mexiletine, 200 mg, and phenytoin, 100 mg, three times daily; this combination achieved the best result but with a ventricular rate still 120/min.

Two months later severe congestive heart failure recurred despite treatment with spironolactone, 150 mg daily, and frusemide, 160 mg daily. In November 1973 amiodarone was obtained from the Belgian manufacturer (Labaz), and the patient started taking 200 mg by mouth thrice daily. Within a few days the ventricular rate fell, and sinus rhythm supervened on the 14th day of treatment (see figure). The heart failure improved rapidly. The dose of amiodarone was reduced progressively, and the patient has remained well, fully active, and free from failure, receiving amiodarone, 200 mg, on alternate days and hydrochlorothiazide and amiloride (Moduretic), one tablet daily. Regular slit-lamp examinations of the corneae have shown only trivial changes.

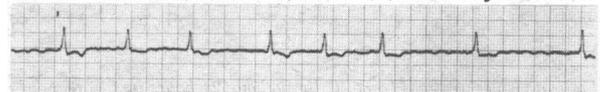
**Comment**

Amiodarone is not related to other antiarrhythmic drugs in common use. It was introduced to treat angina, but later powerful anti-

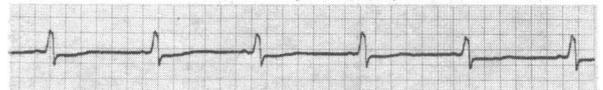
19 Nov '73 On mexiletine & phenytoin



25 Nov '73 Amiodarone 200mg thrice daily. Other drugs discontinued



3 Dec '73 Amiodarone 200mg twice daily



All lead II

Top strip: electrocardiogram when patient presented for second time. Heart rate 140/min with WPW complexes. Middle strip: six days after starting amiodarone. Heart rate had slowed considerably and complexes no longer show WPW pattern. Bottom strip: two weeks after starting amiodarone, patient in sinus rhythm but again with aberrant conduction.